European Thyroid Journal

Clinical Thyroidology / Research Article

Eur Thyroid J 2021;10:486–494
DOI: 10.1159/000510620

Received: May 26, 2020
Accepted: August 1, 2020
Published online: September 29, 2020

Long-Term Outcome of Lobectomy for Thyroid Cancer

Matthieu Bosset[a] Maxime Bonjour[b] Solène Castellnou[a]
Zakia Hafdi-Nejjari[c] Claire Bournaud-Salinas[d] Myriam Decaussin-Petrucci[e]
Jean Christophe Lifante[f, g] Agnès Perrin[a] Jean-Louis Peix[f] Philippe Moulin[a, h]
Geneviève Sassolas[c] Michel Pugeat[a] Françoise Borson-Chazot[a, c, g]

[a]Fédération d'Endocrinologie, Hospices Civils de Lyon, Groupement Hospitalier Est, Bron, France; [b]Service de Biostatistique, Hospices Civils de Lyon, Lyon, France; [c]Registre des Cancers Thyroïdiens du Département du Rhône, Hospices Civils de Lyon, Groupement Hospitalier Est, Bron, France; [d]Centre de Médecine Nucléaire, Hospices Civils de Lyon, Groupement Hospitalier Est, Bron, France; [e]Service d'Anatomie-Pathologique, Hospices Civils de Lyon, Groupement Hospitalier Lyon-Sud, Pierre Bénite, France; [f]Service de Chirurgie Endocrinienne, Hospices Civils de Lyon, Groupement Hospitalier Lyon-Sud, Pierre Bénite, France; [g]Laboratoire Health Services and Performance Research (EA 7425 HESPER), Université Claude Bernard Lyon 1, Villeurbanne, France; [h]CarMeN Laboratory, Université Claude-Bernard Lyon 1, Inserm U1060, INRA U1397, INSA Lyon, IMBL, Villeurbanne, France

Keywords
Lobectomy · Thyroid cancer · Cancer recurrence · Thyroid reoperation · Papillary thyroid cancer

Abstract
Introduction: Recent guidelines of the American Thyroid Association (ATA) suggest that a lobectomy may be sufficient to treat low- to intermediate-risk patients with thyroid tumors ≤40 mm, without extrathyroidal extension or lymph node metastases. The present study aimed to evaluate long-term recurrence after lobectomy for differentiated thyroid cancer and to analyze factors associated with recurrence. ***Methods:*** In this retrospective cohort study, patients who underwent a lobectomy for thyroid cancer in a tertiary center between 1970 and 2010 were included. The outcome was the proportion of pathology-confirmed thyroid cancer recurrence, assessed in the whole cohort or in subgroups according to tumor size (≤ or >40 mm). ***Results:*** A total of 295 patients were included, and these were followed-up for a mean (standard deviation, SD) 19.1 (7.8) years (5,649 patient-years); 61 (20.7%) were male and the mean (SD) age at diagnosis was 39.7 (12) years. Histological subtype was papillary in 263 (89.2%) patients and mean cancer size was 22.9 (16.9) mm. According to the 2015 ATA guidelines, 271 (91.9%) cancers had a low risk of recurrence and 24 (8.1%) an intermediate risk. A reoperation was performed in 54 patients (18.3%) and recurrence was confirmed in 40 (13.6%), diagnosed for 55% of cases more than 10 years after their initial surgery. Among recurrent patients, 14 (4.8% of the cohort) were operated for a contralateral papillary thyroid microcarcinoma and 26 (8.8% of the cohort) for a locoregional or metastatic recurrence. Non-suspicious nodular recurrences were monitored without reoperation in 53 (18.0%) patients. At the end of follow-up, 282 (95.6%) patients were in remission. Tumors with locoregional or metastatic recurrence were more fre-

karger@karger.com
www.karger.com/etj

Solène Castellnou
Fédération d'Endocrinologie, Groupement Hospitalier Est, Hospices Civils de Lyon
59 Boulevard Pinel
FR–69500 Bron (France)
solene.castellnou@chu-lyon.fr

quent among tumors with aggressive histology (19.2 vs. 4.1%, $p = 0.015$) and of intermediate risk category (28.6 vs. 7.1%, $p = 0.018$). Tumors >40 mm, which would have been treated by thyroidectomy according to the 2015 ATA guidelines criteria, were found in 34 (11.5%) patients and were associated with a higher frequency of recurrence (20.6 vs. 7.3%, $p = 0.024$) and less remission (85.3 vs. 96.9%, $p = 0.001$). ***Conclusion:*** The outcome of thyroid cancer treated by lobectomy is very good, particularly for cancer ≤40 mm. A prolonged follow-up is required due to the risk of late recurrence.

Introduction

Thyroid cancer is the most common endocrine malignancy, and its incidence globally has increased over the last 30 years [1, 2]. Papillary thyroid cancer (PTC) represents more than 90% of all thyroid cancer cases and is the most indolent form of the disease [3]. Prognosis is excellent as the 20-year survival is over 90% [4]. Risk factors are histology, extent of disease, and size of the tumor, and more than two-thirds of patients have low-risk cancer [5, 6]. The mainstay of PTC treatment is surgical resection which allows removal of the tumor, perform histology, and classify patients (4–5). Lobectomy was performed in our center mostly during the eighties and early nineties. Total thyroidectomy, which has been associated with increased overall survival [7] and lower risk of recurrence [8, 9] in some studies, then became the treatment of choice. However, it is also followed by hypothyroidism and there is a risk of surgical complications such as hypoparathyroidism or recurrent laryngeal nerve paralysis, which can affect patients' quality of life [10]. Currently, this practice is being questioned as a number of cohort studies have suggested that thyroid lobectomy may be sufficient in low- to intermediate-risk patients, the extent of initial thyroid surgery having no impact on disease-specific survival for these patients [11–16]. Contrary to previous guidelines which indicated lobectomy for small (<1 cm), unifocal, intrathyroidal, node-negative, low-risk tumors [17], the 2015 American Thyroid Association (ATA) guidelines have allowed to perform lobectomy in low- to intermediate-risk patients (patients with unifocal tumors <4 cm, and no evidence of extrathyroidal extension or lymph node metastases upon examination or imaging) [5]. However, this is still controversial, as a recently published systematic review found a small but significantly higher recurrence rate after lobectomy than thyroidectomy for low-risk well-differentiated thyroid cancer [18], and more data are needed for intermediate-risk tumors [19–21]. This confirms that the long-term prognosis of those tumors still needs to be assessed. The aims of the present study were to describe the recurrence rate and long-term outcomes of patients who underwent a lobectomy for differentiated thyroid cancer, for all patients or according to tumor size (≤ or >40 mm), and to analyze factors associated with recurrence.

Material and Methods

Patient Selection and Follow-Up

This was a retrospective cohort study of consecutive patients who underwent a thyroid lobectomy for differentiated thyroid cancer, between 1970 and 2010 in a tertiary endocrinology center. Data from a hospital database were used for this study. Inclusion criteria were a documented histology, at least one cervical ultrasound performed during the follow-up and a follow-up of >5 years for those without recurrence. Patients with postoperative thyroid completion, anaplastic thyroid cancer, or medullary thyroid cancer were excluded. Histological subtypes of thyroid cancer were separated into non-aggressive forms that include classic PTC, follicular PTC variant, and well-differentiated follicular thyroid cancer versus aggressive forms that include poorly differentiated carcinoma, diffuse sclerosing PTC variant, solid/trabecular PTC variant, and Hürthle (oncocytic) thyroid cancer. Patient and tumor characteristics, such as tumor size and TNM, based on the seventh edition of American Joint Committee on Cancer/Union for International Cancer Control TNM classification system, were reported into the database and all thyroid cancers were retrospectively categorized using the 2015 ATA guidelines as being at low, intermediate, or high risk of recurrence [5]. All patients over the study period were to be followed at least each year following surgery by clinical examination and laboratory tests. Monitoring procedures changed over the study period and thyroglobulin was to be measured regularly since 1990. Ultrasounds were initially performed at the discretion of the attending physician, while in recent years ultrasounds were to be performed annually during the first 5 years or if abnormalities and every 3–5 years thereafter. All patients were to receive levothyroxine postoperatively; the objective was to obtain a TSH in accordance with the guidelines in place at that time. As TSH and thyroglobulin assay techniques evolved over time, these parameters were interpreted according to standards in place. Thyroglobulin was considered stable in the absence of plasma concentration doubling within 2 years. Reoperations were performed if thyroid nodules or cervical lymph nodes were discovered or increased in size, along with a suspicious ultrasound result and positive or suspicious fine needle cytology aspiration finding. In case of reoperations, a lymph node dissection was performed only if a metastatic lymph node was suspected. Radioactive iodine treatment was added if cancer recurrence was confirmed.

Outcome

The primary outcome was the proportion of pathology-confirmed thyroid cancer recurrence. Two analyses were carried out:

Table 1. Patient and tumor characteristics in the total cohort (n = 295) and according to recurrence

	Total population n = 295	Recurrence		p value*	Locoregional or metastatic recurrence (excluding contralateral micro-PTC)		p value*
		no n = 255	yes n = 40		no n = 269	yes n = 26	
Gender							
Male	61	50 (82.0)	11 (18.0)	0.349	53 (86.9)	8 (13.1)	0.282
Female	234	205 (87.6)	29 (12.4)		216 (92.3)	18 (7.7)	
Age at surgery, mean (SD), years	39.8 (12)	39.9 (11.9)	38.9 (13.0)	0.618	39.7 (12.0)	40.6 (12.7)	0.716
Histological subtype							
PTC	263	227 (86.3)	36 (13.7)	0.533	241 (91.6)	22 (8.4)	0.302
FTC	29	26 (89.7)	3 (10.3)		26 (89.7)	3 (10.3)	
Oncocytic	3	2 (66.7)	1 (33.3)		2 (66.7)	1 (33.3)	
Prognosis of histological subtype							
Non-aggressive	279	244 (87.5)	35 (12.5)	0.141	258 (92.5)	21 (7.5)	**0.015**
Aggressive	16	11 (68.8)	5 (31.2)		11 (68.8)	5 (31.2)	
Tumor size, mean (SD), mm	22.9 (16.9)	22.6 (16.6)	25.1 (18.7)	0.383	22.4 (16.6)	28.9 (18.8)	0.059
T staging[a]							
T1	145	123 (84.8)	22 (15.2)	**0.014**	134 (92.4)	11 (7.6)	**0.026**
T2	110	102 (92.7)	8 (7.3)		103 (93.6)	7 (6.4)	
T3	40	30 (75.0)	10 (25.0)		32 (80.0)	8 (20.0)	
Unifocal cancer	226	196 (86.7)	30 (13.3)	0.92	205 (90.7)	21 (9.3)	0.802
Risk of recurrence[b]							
Low	271	237 (87.5)	34 (12.5)	0.162	251 (92.6)	20 (7.4)	**0.011**
Intermediate	24	18 (75.0)	6 (25.0)		18 (75.0)	6 (25.0)	
Follow-up time, years, mean (SD)	19.15 (7.76)	18.97 (7.52)	20.27 (9.17)	0.327	18.91 (7.48)	21.65 (10.02)	0.085

Data reported as counts (percentages in line) unless otherwise specified. SD, standard deviation; PTC, papillary thyroid cancer; FTC, follicular thyroid cancer; ATA, American Thyroid Association; AJCC/UICC, American Joint Committee on Cancer/Union for International Cancer Control. * p value calculated using Student's t test for quantitative data and χ^2 test for qualitative data. [a] Staging according to the seventh edition of the AJCC/UICC TNM classification system. [b] Risk of recurrence categorized using the 2015 ATA guidelines.

either all recurrences were taken into account (recurrence group) or only a subset of patients excluding those whose recurrence was a contralateral micro-PTC. This second group included only patients with locoregional recurrence (lymph nodes or/and operated thyroid bed) or metastasis. Secondary outcome was the final status of patients: remission, persistent disease, or undetermined status. Patients were considered to be in remission if, after >5 years of follow-up, no signs of recurrence were found, or if there were no signs of recurrence during follow-up in reoperated patients with benign histology, or after >5 years of remission in reoperated patient with recurrence; patients with monitored thyroid nodule or cervical lymph node but without suspicious characteristics on ultrasound, with negative fine needle cytology aspiration results and a stable thyroglobulin were also classified in the remission group. Patients with recurrence were considered to have persistent disease in cases of persistence of a local or metastatic suspicious structural element (structural persistent disease) or in case of positive thyroglobulin (biochemical persistent disease) in the absence of localizable disease. Patients were considered to have undetermined status if, after a recurrence, the follow-up period was <5 years.

Statistics

Quantitative data are presented as mean and standard deviation and qualitative data are presented as count and percentage (%). For the bivariate analysis, continuous variables were compared between patients with and without thyroid cancer recurrence/locoregional or metastatic recurrence (excluding micro-PTC), and between tumors ≤40 and >40 mm using Student's t test, while categorical variables were compared using the χ^2 test. To evaluate the association between the patient/tumor characteristics and the probability to have a locoregional or metastatic thyroid cancer recurrence, multivariate logistic regression analysis was conducted. Two-sided p values <0.05 were considered as significant.

Ethical Considerations

The study was approved by the institutional ethics committee (*Comité d'Éthique du CHU de Lyon, no.* 16-01) in accordance with French legislation in place at the time of the study.

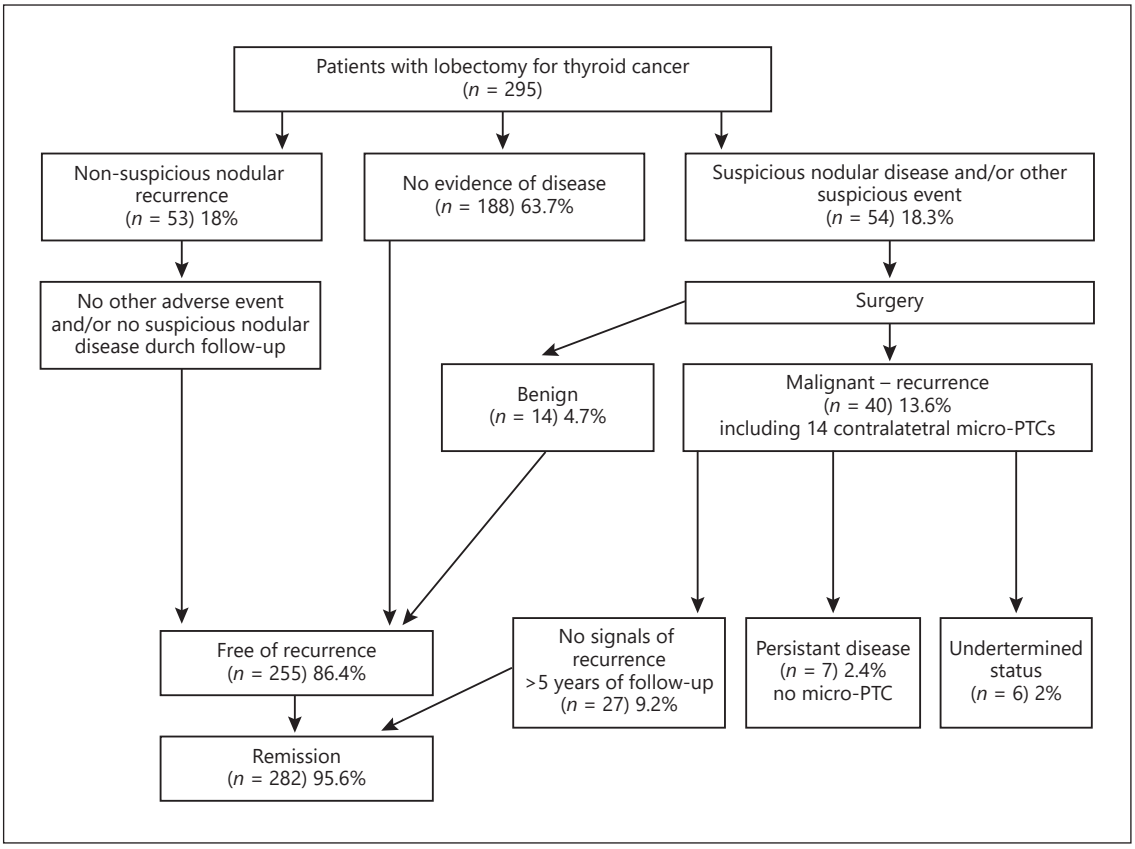

Fig. 1. Outcome of the 295 patients who underwent thyroid lobectomy between 1970 and 2010. PTC, papillary thyroid cancer.

Results

Population Characteristics

A total of 372 patients underwent a thyroid lobectomy for differentiated thyroid cancer between 1970 and 2010. Among these, 41 had short follow-up (<5 years), 15 had incomplete histology, and 21 had missing ultrasounds. Therefore, a total of 295 patients were included in the study. Median year of surgery was 1989 (range: 1971–2010). A minority (20.7%) of patients were male and the mean age at surgery was 39.8 (12) years. After lobectomy, a recurrent laryngeal nerve paralysis was found in 5 (1.7%) patients. Regarding thyroid cancer characteristics, 263 (89.2%) were PTC, the mean cancer size was 22.9 (16.9) mm, and 226 (76.6%) were unifocal. According to the 2015 ATA guidelines, 271 (91.9%) thyroid cancers had low risk of recurrence, and 24 (8.1%) had an intermediate risk of recurrence. No cancer had a high risk of recurrence (Table 1).

Follow-Up

Patients were followed-up for a mean of 19.1 (7.8) years, representing 5.649 patient-years. Overall, 87.2% of patients were followed for at least 10 years, and 46.1% for at least 20 years. Among the 295 patients, 255 were free of recurrence. Fifty three (18.0%) patients were monitored for non-suspicious nodular recurrence in the contralateral lobe, while a thyroid reoperation was performed for 54 patients, representing a reoperation rate of 18.3%. Among the 54 patients with reoperation, recurrence was confirmed following pathology analysis in 40 patients (13.6% of the cohort), including 14/40 (4.8% of the cohort) patients operated for contralateral micro-PTC and 26/40 (8.8% of the cohort) patients operated for a locoregional or metastatic recurrence. Among reoperated patients, 14 (4.8% of the cohort) had a benign histology, representing 25.9% of all reoperations. At the end of follow-up, 282 (95.6%) patients were in remission and a persistent disease was present in 7 (2.4%) patients (Fig. 1), including 1 patient who died from thyroid cancer. This

Table 2. Multivariate analysis of preoperative factors that may influence the occurrence of a true recurrence

	b (estimate)	SE (estimate)	OR	*p* value
Gender				
Female	0		1	0.281
Male	0.504	0.467	1.655	
Age at surgery, years	0.007	0.018	1.007	0.717
Histological subtype				
Non-papillary	0		1	0.867
Papillary	0.112	0.668	1.118	
Cancer focality				
Multifocal	0		1	0.714
Unifocal	0.195	0.531	1.215	
Risk of recurrence[a]				
Low	0		1	**0.020**
Intermediate	1.372	0.591	3.944	
Follow-up time, years	0.041	0.027	1.042	0.130

SE, standard error; OR, odds ratio; ATA, American Thyroid Association. [a] Risk of recurrence categorized using the 2015 ATA guidelines.

patient was initially operated for a poorly differentiated follicular thyroid cancer of 55 mm, with an intermediate risk of recurrence.

Characteristics of Recurrences

When taking into account all recurrences, patients were operated after a mean of 13.5 (8.8) years following their first intervention; 7/40 (17.5%) during the first 5 years, 11/40 (27.5%) between 5 and 10 years, and 22/40 (55%) after 10 years. Among patients operated more than 10 years after their first intervention, 7/22 were operated for a contralateral micro-PTC and 15/22 for a locoregional or a metastatic recurrence. Nineteen (47.5%) patients had an effective hormone replacement therapy treatment; TSH was undetectable at the time of recurrence. In univariate analysis, the only significant difference between patients with and without recurrence (including patients with contralateral micro-PTC) was the distribution of the pT staging ($p = 0.014$) with a higher number of pT3 tumors among recurrent patients (10/40 = 25% vs. 30/255 = 11.8%). Among the 40 patients with recurrence, 26 were not contralateral micro-PTC, 23 (88.5%) being locoregional, and 3 (11.5%) metastatic. Compared to patients without locoregional or metastatic recurrence, the tumors of those with locoregional or metastatic recurrence were more often aggressive (5/26 = 19.2% vs. 11/269 = 4.1%, $p = 0.015$) and at intermediate risk according to the 2015 ATA guidelines (6/26 = 23.1% vs. 18/269 = 6.7%, $p = 0.011$). In patients with locoregional or metastatic recurrence compared to the others, distribution of the pT staging was significantly different ($p = 0.026$) with a higher number of pT3 tumors (8/26 = 30.8% vs. 32/269 = 11.9%) and a trend towards a larger mean tumor size (28.9 vs. 22.4 mm, $p = 0.059$) was found (Table 1). In multivariate analysis, the only factor significantly associated with locoregional or metastatic recurrence was the risk of recurrence according to the 2015 ATA guidelines ($p = 0.02$, Table 2).

Outcomes Assessment after Revision of the Type of Surgery Indicated according to the 2015 ATA Criteria

Among the 295 patients who underwent a thyroid lobectomy between 1970 and 2010, 34 (11.5%), with a tumor size >40 mm, would have had a thyroidectomy instead of a lobectomy according to the 2015 ATA guidelines criteria. Compared to those with a smaller tumor, those with a tumor >40 mm had a higher reoperation rate (11/34 = 32.4% vs. 43/261 = 16.5%, $p = 0.044$) and had a greater number of recurrences (9/34 = 26.5% vs. 31/261 = 11.9%, $p = 0.038$) as well as locoregional or metastatic recurrences (7/34 = 20.6% vs. 19/261 = 7.3%, $p = 0.024$). No metastasis was found among patients with a tumor size ≤40 mm. At the end of the follow-up, the duration of which did not differ significantly between the 2 groups, 29/34 (85.3%) patients with a tumor size >40 mm were in remission compared to 253/261 (96.9%) patients with a smaller tumor ($p = 0.001$, Table 3).

Table 3. Outcome evaluation depending on the initial tumor size

	Total population $n = 295$	Tumor size		p value*
		≤40 mm $n = 261$	>40 mm $n = 34$	
Duration of follow-up, mean (SD), years	19.15 (7.76)	19.11 (7.62)	19.44 (8.90)	0.815
Reoperation	54	43 (79.6)	11 (20.4)	**0.044**
Recurrence	40	31 (77.5)	9 (22.5)	**0.038**
Type of recurrence				
Locoregional	23	19 (82.6)	4 (17.4)	**0.004**
Metastasis	3	0 (0.0)	3 (100.0)	
Contralateral micro-PTC	14	12 (85.7)	2 (14.3)	
Locoregional or metastatic recurrence	26	19 (73.1)	7 (26.9)	**0.024**
Final status				
Undetermined	6	5 (83.3)	1 (16.7)	**0.001**
Persistent disease	7	3 (42.9)	4 (57.1)	
Remission	282	253 (89.7)	29 (10.3)	

Data reported as counts (percentages in line) unless otherwise specified. SD, standard deviation; PTC, papillary thyroid cancer. * p value calculated using Student's t test for quantitative data and χ^2 test for qualitative data.

Discussion

The present study, based on a large number of cases of differentiated thyroid cancers treated by thyroid lobectomy, found a very good outcome after lobectomy after a long follow-up. Furthermore, after distinguishing patients according to current ATA guidelines and thus tumor size, outcome was even better for tumors ≤40 mm.

The recurrence rate and locoregional and metastatic recurrence rate herein were slightly higher than that previously reported after lobectomy, ranging from 4.2 to 7.1% [11–13, 22, 23]. This could be explained by the fact that the cohort is older than other studies [11–13] and that preoperative assessment of thyroid cancers was probably less reliable at the beginning of the study period, ultrasonography being less sensitive than currently. The present study also has a very long follow-up period compared to some other studies [11, 12, 22, 23], which allowed us to detect late recurrences. The high number of late recurrences found herein, more than half of patients being reoperated more than 10 years after initial diagnosis, demonstrates that a long period of follow-up is needed. While some retrospective cohorts were composed of only well differentiated low-risk PTC [13, 22, 23], the present study also included patients of intermediate risk of recurrence, with aggressive histological subtype, and with cancer >40 mm. Recurrence rate was higher in tumors >40 mm. This finding supports current guidelines, as patients with tumors >40 mm or those classified in the ATA intermediate risk category after pathology results would likely have benefited from a thyroidectomy or would undergo a thyroid completion following current criteria. However, it is important to note that a certain number of lobectomies may have been performed for Noninvasive Follicular Thyroid Neoplasm with Papillary-like nuclear Features instead of follicular PTC variant. This recently identified entity, which is to be distinguished from thyroid cancer, is known to be of excellent prognosis and could artificially decrease the recurrence rate after lobectomy observed in the present study and other studies [24, 25].

Herein, 40% of recurrences were contralateral micro-PTCs, and all were in remission at the end of follow-up. Micro-PTCs are known to have a low evolutionary potential with a very good prognosis and could benefit from active surveillance instead of surgery [4, 26, 27]. Their incidence is increasing as they are often found fortuitously, leading to an overdiagnosis of thyroid cancers [4, 28–30]. In line with the present results, contralateral carcinomas have been previously found in a third of patients operated for thyroid cancer and predominantly consisted of micro-PTCs independently of primary tumor subtype [31]. Such contralateral micro-PTCs as those described herein could thus be fortuitous discoveries favored by the close follow-up of patients. Another hypothesis is that, PTCs being often multifocal [32, 33], micro-nodules could have been present in the contralateral lobe at the time of diagnosis, but might have gone undetected due to the lower sensitivity of the ultrasound technique used for

part of the study period. Concerning multifocal cancers, a higher rate of those was reported in previous studies than that observed on pathology analysis herein [32, 33]. This could be due to an underestimation of the bilateral multifocal cancer when performing lobectomies as well as an evolution of the pathology analysis technique which is now based on a higher number of samples per lobe [34].

It has been reported than the overall survival of low-risk patients who underwent lobectomy was similar to that of patients with thyroidectomy [15, 16, 35–37]. The very low mortality rate found herein is consistent with previous findings [13, 14, 37], and this even though the present study included patients who would currently be managed by thyroidectomy, such as the only patient reported in the present study who died of his thyroid cancer. Overall, this supports the current guidelines suggesting that for patients with low- to intermediate risk and tumor ≤40 mm, the extent of initial thyroid surgery likely has little impact on disease-specific survival [5]. Thyroidectomy, followed by radioactive iodine therapy, is known to facilitate monitoring through the surveillance of thyroglobulin [17]. However, the use of thyroglobulin as a guide for cancer recurrence after lobectomy has been previously reported [38,39] and a more recent study has shown that an increase in unstimulated thyroglobulin could help identify cancer recurrence [40]. Lobectomy may be considered as an interesting alternative for selected patients, as fewer postoperative complications are generally expected after this procedure than in a thyroidectomy [10, 16], although a previous review found a similar complication rate for both surgical procedures [41]. However, the realization of a lobectomy requires a regular and prolonged follow-up which can be complicated by non-suspicious nodular recurrences, as found herein in approximately one-fifth of patients. This proportion of non-suspicious nodular recurrences is consistent with the relatively high prevalence of goiter in France, which is favored by insufficient Iodine intake [42–44]. Of note, the potential absence of postoperative hormone supplementation is not a good argument to guide surgical decision since L-thyroxine treatment is also often prescribed after lobectomy, as it was the case herein for all patients; this is currently indicated to supplement hypothyroidism [45], but this was also widely used in the past in France to prevent the occurrence of new nodules or thyroid cancer recurrence [39,46]. In addition, it may be useful to consider the economic impact of the surgical strategy. It has previously been suggested that taking into account long-term follow-up and treatment of recurrence, total thyroidectomy may be more cost-effective than lobectomy [47].

This single-center study, although retrospective, has the advantage of a long follow-up which allowed studying an important number of consecutive cases treated by lobectomy. However, this long period of study also entails that an important evolution of monitoring procedures occurred between 1970 and 2010. The absence of a control group treated by thyroidectomy did not allow us to compare the outcomes of the 2 surgical procedures. Further studies are needed and the HoT trial, a randomized controlled trial recently funded in the UK and which aims to compare outcomes by extent of thyroid surgery in low-risk differentiated thyroid cancer, will be helpful to refine the results reported herein.

Conclusion

After a proper selection of patients, currently based on the 2015 ATA guidelines, lobectomy shows excellent clinical outcomes. Although it is associated with lower postoperative complications than total thyroidectomy, the risk of contralateral nodular recurrence and late recurrences requiring prolonged follow-up should be taken into account.

Acknowledgements

We thank Philip Robinson and Véréna Landel for help in manuscript preparation.

Statement of Ethics

In accordance with French legislation for observational studies in force at the time of the study, patients were informed about the study and were not included if they objected; however, written consent was not required (MR-003). The study was approved by the institutional ethics committee (*Comité d'Éthique du CHU de Lyon, n°*. 16-01).

Conflict of Interest Statement

The authors have nothing to disclose in the area of the study.

Funding Sources

This research did not receive any specific grant from any funding agency in the public, commercial, or not-for-profit sector.

Author Contributions

Conceptualization: Françoise Borson-Chazot, Michel Pugeat, and Matthieu Bosset; methodology: Françoise Borson-Chazot, Matthieu Bosset, and Maxime Bonjour; Statistical analysis: and Maxime Bonjour; writing – original draft preparation: Matthieu Bosset, Solène Castellnou, and Françoise Borson-Chazot; writing – review and editing: Maxime Bonjour, Zakia Hafdi-Nejjari, Claire Bournaud-Salinas, Myriam Decaussin-Petrucci, Jean-Christophe Lifante, Agnès Perrin, Jean-Louis Peix, Philippe Moulin, Geneviève Sassolas, and Michel Pugeat. All authors have read and agreed to the published version of the manuscript.

References

1 La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F, et al. Thyroid cancer mortality and incidence: a global overview. Int J Cancer. 2015 May;136(9):2187–95.

2 Chen AY, Jemal A, Ward EM. Increasing incidence of differentiated thyroid cancer in the United States, 1988–2005. Cancer. 2009 Aug;115(16):3801–7.

3 Leboulleux S, Tuttle RM, Pacini F, Schlumberger M. Papillary thyroid microcarcinoma: time to shift from surgery to active surveillance? Lancet Diabetes Endocrinol. 2016 Nov;4(11):933–42.

4 Colonna M, Uhry Z, Guizard AV, Delafosse P, Schvartz C, Belot A, et al. Recent trends in incidence, geographical distribution, and survival of papillary thyroid cancer in France. Cancer Epidemiol. 2015 Aug;39(4):511–8.

5 Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American thyroid association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016 Jan;26(1):1–133.

6 Lamartina L, Grani G, Durante C, Borget I, Filetti S, Schlumberger M. Follow-up of differentiated thyroid cancer: what should (and what should not) be done. Nat Rev Endocrinol. 2018; 14(9): 538–51. https: //doi.org/10.1038/s41574-018-0068-3.

7 Bilimoria KY, Bentrem DJ, Ko CY, Stewart AK, Winchester DP, Talamonti MS, et al. Extent of surgery affects survival for papillary thyroid cancer. Ann Surg. 2007 Sep;246(3):375–4.

8 Grant CS, Hay ID, Gough IR, Bergstralh EJ, Goellner JR, McConahey WM. Local recurrence in papillary thyroid carcinoma: is extent of surgical resection important? Surgery. 1988 Dec;104(6):954–62. https://doi.org/10.5555/uri:pii:0039606088901547.

9 Hay ID, Grant CS, Bergstralh EJ, Thompson GB, van Heerden JA, Goellner JR. Unilateral total lobectomy: is it sufficient surgical treatment for patients with AMES low-risk papillary thyroid carcinoma? Surgery. 1998 Dec;124(6):958–6.

10 Ryu J, Ryu YM, Jung YS, Kim SJ, Lee YJ, Lee EK, et al. Extent of thyroidectomy affects vocal and throat functions: a prospective observational study of lobectomy versus total thyroidectomy. Surgery. 2013 Sep;154(3):611–20.

11 Vaisman F, Momesso D, Bulzico DA, Pessoa CH, da Cruz MD, Dias F, et al. Thyroid lobectomy is associated with excellent clinical outcomes in properly selected differentiated thyroid cancer patients with primary tumors greater than 1 cm. J Thyroid Res. 2013;2013:398194.

12 Vaisman F, Shaha A, Fish S, Michael Tuttle R. Initial therapy with either thyroid lobectomy or total thyroidectomy without radioactive iodine remnant ablation is associated with very low rates of structural disease recurrence in properly selected patients with differentiated thyroid cancer. Clin Endocrinol. 2011 Jul;75(1):112–9.

13 Matsuzu K, Sugino K, Masudo K, Nagahama M, Kitagawa W, Shibuya H, et al. Thyroid lobectomy for papillary thyroid cancer: long-term follow-up study of 1,088 cases. World J Surg. 2014 Jan;38(1):68–79.

14 Barney BM, Hitchcock YJ, Sharma P, Shrieve DC, Tward JD. Overall and cause-specific survival for patients undergoing lobectomy, near-total, or total thyroidectomy for differentiated thyroid cancer. Head Neck. 2011 May;33(5):645–9.

15 Mendelsohn AH, Elashoff DA, Abemayor E, St John MA. Surgery for papillary thyroid carcinoma: is lobectomy enough? Arch Otolaryngol Head Neck Surg. 2010 Nov;136(11):1055–61.

16 Adam MA, Pura J, Goffredo P, Dinan MA, Hyslop T, Reed SD, et al. Impact of extent of surgery on survival for papillary thyroid cancer patients younger than 45 years. J Clin Endocrinol Metab. 2015 Jan;100(1):115–21.

17 American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer; Cooper DS, Cooper DS, Doherty GM, Haugen BR, Hauger BR, et al. Revised American thyroid association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009 Nov;19(11):1167–214.

18 Chan S, Karamali K, Kolodziejczyk A, Oikonomou G, Watkinson J, Paleri V, et al. Systematic review of recurrence rate after hemithyroidectomy for low-risk well-differentiated thyroid cancer. Eur Thyroid J. 2020 Feb;9(2):73–84.

19 Choi JB, Lee SG, Kim MJ, Kim TH, Ban EJ, Lee CR, et al. Oncologic outcomes in patients with 1-cm to 4-cm differentiated thyroid carcinoma according to extent of thyroidectomy. Head Neck. 2019;41(1):56–63.

20 Liu J, Zhang Z, Huang H, Xu S, Liu Y, Liu S, et al. Total thyroidectomy versus lobectomy for intermediate-risk papillary thyroid carcinoma: a single-institution matched-pair analysis. Oral Oncol. 2019 Mar;90:17–22.

21 Tsui KP, Kwan WY, Chow TL. Total vs hemithyroidectomy for intermediate risk papillary thyroid cancer: a 23 year retrospective study in a tertiary center. Am J Otolaryngol. 2019 Jun;40(3):431–4.

22 Kuba S, Yamanouchi K, Hayashida N, Maeda S, Adachi T, Sakimura C, et al. Total thyroidectomy versus thyroid lobectomy for papillary thyroid cancer: comparative analysis after propensity score matching: a multicenter study. Int J Surg. 2017 Feb;38:143–8.

23 Kim MJ, Lee M-C, Lee GH, Choi HS, Cho SW, Kim S-J, et al. Extent of surgery did not affect recurrence during 7-years follow-up in papillary thyroid cancer sized 1–4 cm: preliminary results. Clin Endocrinol. 2017 Jul;87(1):80–6. https://doi.org/10.1111/cen.13336.

24 Xu B, Tallini G, Scognamiglio T, Roman BR, Tuttle RM, Ghossein RA. Outcome of large noninvasive follicular thyroid neoplasm with papillary-like nuclear features. Thyroid. 2017;27(4):512–7.

25 Nikiforov YE, Seethala RR, Tallini G, Baloch ZW, Basolo F, Thompson LD, et al. Nomenclature revision for encapsulated follicular variant of papillary thyroid carcinoma: a paradigm shift to reduce overtreatment of indolent tumors. JAMA Oncol. 2016 Aug 01;2(8):1023–9.

26 Miyauchi A, Ito Y, Oda H. Insights into the management of papillary microcarcinoma of the thyroid. Thyroid. 2018 Jan;28(1):23–31.

27 Ito Y, Miyauchi A, Kihara M, Higashiyama T, Kobayashi K, Miya A. Patient age is significantly related to the progression of papillary microcarcinoma of the thyroid under observation. Thyroid. 2014 Jan;24(1):27–34.

28 Brito JP, Al Nofal A, Montori VM, Hay ID, Morris JC. The impact of subclinical disease and mechanism of detection on the rise in thyroid cancer incidence: a population-based study in Olmsted County, Minnesota during 1935 through 2012. Thyroid. 2015 Sep;25(9):999–1007.

29 Wiltshire JJ, Drake TM, Uttley L, Balasubramanian SP. Systematic review of trends in the incidence rates of thyroid cancer. Thyroid. 2016;26(11):1541–52.

30 Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L. Worldwide thyroid-cancer epidemic? The increasing impact of overdiagnosis. N Engl J Med. 2016 Aug; 375(7):614–7.
31 Lodewijk L, Kluijfhout WP, Kist JW, Stegeman I, Plukker JT, Nieveen van Dijkum EJ, et al. Characteristics of contralateral carcinomas in patients with differentiated thyroid cancer larger than 1 cm. Langenbecks Arch Surg. 2016 May;401(3):365–73.
32 Chow SM, Law SC, Chan JK, Au SK, Yau S, Lau WH. Papillary microcarcinoma of the thyroid-Prognostic significance of lymph node metastasis and multifocality. Cancer. 2003 Jul;98(1):31–40.
33 Tam AA, Özdemir D, Çuhacı N, Başer H, Aydın C, Yazgan AK, et al. Association of multifocality, tumor number, and total tumor diameter with clinicopathological features in papillary thyroid cancer. Endocrine. 2016 Sep;53(3):774–83.
34 Hafdi-Nejjari Z, Abbas-Chorfa F, Decaussin-Petrucci M, Berger N, Couray-Targe S, Schott A-M, et al. Impact of thyroid surgery volume and pathologic detection on risk of thyroid cancer: a geographical analysis in the Rhône-Alpes region of France. Clin Endocrinol. 2018 Dec;89(6):824–33. https://doi.org/10.1111/cen.13833.
35 Haigh PI, Urbach DR, Rotstein LE. Extent of thyroidectomy is not a major determinant of survival in low- or high-risk papillary thyroid cancer. Ann Surg Oncol. 2005 Jan;12(1):81–9.
36 Vargas-Pinto S, Romero Arenas MA. Lobectomy compared to total thyroidectomy for low-risk papillary thyroid cancer: a systematic review. J Surg Res. 2019 Oct;242:244–51.
37 Adam MA, Pura J, Gu L, Dinan MA, Tyler DS, Reed SD, et al. Extent of surgery for papillary thyroid cancer is not associated with survival: an analysis of 61,775 patients. Ann Surg. 2014 Oct;260(4):601.
38 Harvey RD, Matheson NA, Grabowski PS, Rodger AB. Measurement of serum thyroglobulin is of value in detecting tumour recurrence following treatment of differentiated thyroid carcinoma by lobectomy. Br J Surg. 1990 Mar;77(3):324–6.
39 Société Française d'Endocrinologie.. Conférence de consensus: prise en charge des cancers thyroïdiens différenciés de souche vésiculaire. Ann Endocrinol. 2007;68(2):53–56. https://doi.org/10.1016/S0003-4266(07)78635-3.
40 Momesso DP, Vaisman F, Yang SP, Bulzico DA, Corbo R, Vaisman M, et al. Dynamic risk stratification in patients with differentiated thyroid cancer treated without radioactive iodine. J Clin Endocrinol Metab. 2016 Jul; 101(7):2692–700.
41 Cirocchi R, Trastulli S, Randolph J, Guarino S, Di Rocco G, Arezzo A, et al. Total or near-total thyroidectomy versus subtotal thyroidectomy for multinodular non-toxic goitre in adults. Cochrane Database Syst Rev. 2015 Aug;(8):CD010370.
42 Zimmermann MB, Andersson M. Prevalence of iodine deficiency in Europe in 2010. Ann Endocrinol. 2011 Apr;72(2):164–6.
43 Barrère X, Valeix P, Preziosi P, Bensimon M, Pelletier B, Galan P, et al. Determinants of thyroid volume in healthy French adults participating in the SU.VI.MAX cohort. Clin Endocrinol. 2000 Mar;52(3):273–8.
44 Zimmermann MB, Jooste PL, Pandav CS. Iodine-deficiency disorders. Lancet. 2008 Oct; 372(9645):1251–62.
45 Cox C, Bosley M, Southerland LB, Ahmadi S, Perkins J, Roman S, et al. Lobectomy for treatment of differentiated thyroid cancer: can patients avoid postoperative thyroid hormone supplementation and be compliant with the American thyroid association guidelines? Surgery. 2018;163(1):75–80.
46 Wémeau JL, Sadoul JL, d'Herbomez M, Monpeyssen H, Tramalloni J, Leteurtre E, et al. Guidelines of the French society of endocrinology for the management of thyroid nodules. Ann Endocrinol. 2011 Sep;72(4):251–81.
47 Shrime MG, Goldstein DP, Seaberg RM, Sawka AM, Rotstein L, Freeman JL, et al. Cost-effective management of low-risk papillary thyroid carcinoma. Arch Otolaryngol Head Neck Surg. 2007 Dec;133(12):1245–53.